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Attorney Docket No.: 022013-000160US

Mail Stop Amendment  
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On April 6, 2007

By: [Signature]  
Lon M. Cummings

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

KOLKMAN et al.

Application No.: 10/693,056

Filed: October 24, 2003

For: COMBINATORIAL LIBRARIES OF  
MONOMER DOMAINS

Customer No.: 30174

Confirmation No. 1550

Examiner: Liu

Art Unit: 1639

### INFORMATION DISCLOSURE STATEMENT

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08 is a listing of documents known to Applicants in order to comply with Applicants' duty of disclosure pursuant to 37 CFR §1.56.

A copy of each foreign patent document and non-patent listed reference is being submitted to comply with the provisions of 37 CFR §1.97 and §1.98.

The submission of any document herewith is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.

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Application No. 10/693,056  
Kolkman et al.

Applicants respectfully request that each listed document be considered by the Examiner and be made of record in the present application, and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The information disclosure statement submitted herewith is being filed after the mailing date of the first Office action on the merits, but before the mailing date of either a final action under § 1.113 or a notice of allowance under § 1.311, whichever occurs first.

Please charge Deposit Account No. 01-0519 the amount of \$180.00 as set forth in 37 CFR 1.17(p) for submission of an information disclosure statement under § 1.97(c).

The Commissioner is hereby authorized to charge any additional fees which may be required or credit any overpayment to Deposit Account No. 01-0519 in the name of Amgen Inc.

Respectfully submitted,



Charles K. Sholtz  
Attorney/Agent for Applicant(s)  
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Date: 4-5-2007

Please send all future correspondence to:

Customer Number 30174  
Amgen Inc.  
1120 Veterans Boulevard  
South San Francisco, CA 94080



**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	10/693,056
Filing Date	October 24, 2003
First Named Inventor	Kolkman, et al.
Art Unit	1639
Examiner Name	LIU, Sue Xu

Sheet 1 of 8 Attorney Docket No: 022013-000160US

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD- YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code <sup>2</sup> (if known)			
		US-6140466	10-31-2000	BARBAS, III; Carlos F. et al.	
		US-2004132094A1	07-08-2004		
		US-20050053973	03-10-2005	KOLKMAN; Joost A. et al.	
		US-20050089932	04-28-2005	KOLKMAN; Joost et al.	
		US-20050221384	10-06-2005	KOLKMAN; Joost A. et al.	
		US-20060008844A1	01-12-2006	STEMMER; Willem P. C. et al.	
		US-20060177831	08-10-2006	STEMMER; Willem P. C. et al.	
		US-2006223114A1	10-05-2006	STEMMER; Willem P. C. et al.	
		US-2006234299A1	10-19-2006	STEMMER; Willem P. C. et al.	

**FOREIGN PATENT DOCUMENTS**

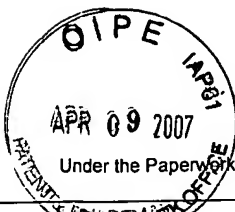
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		Country Code <sup>3</sup> - Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)				
		EP-623679A1	11-09-1994	Micromet Ag		<input type="checkbox"/>
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		WO-0034784	06-15-2000	Phylos, inc.		<input type="checkbox"/>
		WO-0060070	10-12-2000	Innogenetics N.V.		<input type="checkbox"/>
		WO-0075308	12-14-2000	Skerra, Arne		<input type="checkbox"/>
		WO-0127147	04-19-2001	The University of Queensland et al.		<input type="checkbox"/>
		WO-0157065	08-09-2001	Diversys Limited		<input type="checkbox"/>

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		<b>Application Number</b>	10/693,056		
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		<b>First Named Inventor</b>	Kolkman, et al.		
		<b>Art Unit</b>	1639		
		<b>Examiner Name</b>	LIU, Sue Xu		
<b>Sheet</b>	<b>2</b>	<b>of</b>	<b>8</b>	<b>Attorney Docket No:</b> 022013-000160US	

FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> -Kind Code <sup>5</sup> (if known)				
		WO-0177342	10-18-2001	Genentech, Inc.		<input type="checkbox"/>
		WO-0204523	01-17-2002	Research Corporation Technologies, Inc. et al.		<input type="checkbox"/>
		WO-0212277	02-14-2002	Diversys Limited		<input type="checkbox"/>
		WO-0232925	04-25-2002	Phylos, Inc. et al.		<input type="checkbox"/>
		WO-9106305	05-16-1991	Bristol-Myers Squibb Company		<input type="checkbox"/>
		WO-9111461	08-08-1991	Biogen, Inc. et al.		<input type="checkbox"/>
		WO-9117173	11-14-1991	Cytogen Corporation		<input type="checkbox"/>
		WO-9323537	11-25-1993	Creative Biomolecules et al.		<input type="checkbox"/>
		WO-9411403	05-26-1994	Mosbach, Klaus et al.		<input type="checkbox"/>
		WO-9428173	12-08-1994	Affymax Technologies N.V. et al.		<input type="checkbox"/>
		WO-9519567	07-20-1995	The Trustees of Columbia University in the City of New York et al.		<input type="checkbox"/>
		WO-9637621	11-28-1996	Morphosys Gesellschaft fuer Proteinoptimierung MbH et al.		<input type="checkbox"/>
		WO-9721829	06-19-1997	Merck Patent GmbH		<input type="checkbox"/>
		WO-9856906	12-17-1998	Larsen, Ingrid, Kjoller		<input type="checkbox"/>
		WO-9856915	12-17-1998	Research Corporation Technologies, Inc.		<input type="checkbox"/>
		WO-9916873	04-08-1999	Skerra, Arne		<input type="checkbox"/>
		WO-9919276	04-22-1999	ALNIS, LLC et al.		<input type="checkbox"/>
		WO-9945110	09-10-1999	Diatech Pty. Ltd.		<input type="checkbox"/>

## NON PATENT LITERATURE DOCUMENTS

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of

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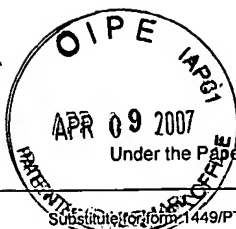
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		SCHULTZ J. et al., SMART: a web-based tool for the study of genetically mobile domains., NucleicAcids Research, 2000, 28 (1), 231-234.	
		SIMMONS T. et al., Human low density lipoprotein receptor fragment. Successful refolding of a functionally active ligand-binding domain produced in Escherichia coli., J. of Biological Chem., 1997, 272 (41), 25531-25536.	
		SKERRA A. et al., Anticalins': a new class of engineered ligand-binding proteins with antibody-like properties., Reviews in Molecular Biotech. ( J Biotechnol.), 2001, 74 (4), 257-275.	
		SKERRA A. et al., Engineered protein scaffolds for molecular recognition., J. of Molecular Recognition, 2000, 13 (4), 167-187.	
		SKERRA A. et al., Lipocalins as a scaffold., Biochimica Biophysica Acta, 2000, 1482 (1-2), 337-350.	
		SPRINGER T. et al., An extracellular beta-propeller module predicted in lipoprotein and scavenger receptors, tyrosine kinases, epidermal growth factor precursor, and extracellular matrix components, J. Md. Bid.(J Mol Biol.), 1998, 283 (4), 837-862.	
		STOCKINGER W. et al., The low density lipoprotein receptor gene family. Differential expression of two alpha2-macroglobulin receptors in the brain., J. of Biological Chem., 1998, 273 (48), 32213-32221.	
		TROMMSDORFF M. et al., Interaction of cytosolic adaptor proteins with neuronal apolipoprotein E receptors and the amyloid precursor protein, J. of Biological Chem., 1998, 273 (50), 33556-33560.	
		VASH B. et al., Three complement-type repeats of the low-density lipoprotein receptor-related protein define a common binding site for RAP, PAI-1, and lactoferrin., Blood, 1998, 92 (9), 3277-3285.	
		WEISS G. et al., Anticalins versus antibodies: made-to-order binding proteins for small molecules. Chemistry and Biology, 2000, 7 (8), R177-R184.	
		WILLNOW T. et al., Genetic deficiency in low density lipoprotein receptor-related protein confers cellular resistance to Pseudomonas exotoxin A. Evidence that this protein is required for uptake and degradation of multiple ligands., J. of Cell Science, 1994, 107 ( Pt 3), 719-726.	
		YAMAZAKI H. et al., Elements of neural adhesion molecules and a yeast vacuolar protein sorting receptor are present in a novel mammalian low density lipoprotein receptor family member, J. of Biological Chem., 1996, 271 (40), 24761-2478.	

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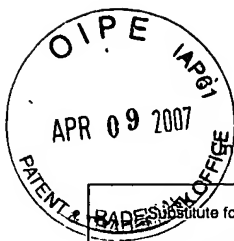
NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T2	
		OBERMOELLER-MCCORMICK L. et al., Dissection of receptor folding and ligand-binding property with functional minireceptors of LDL receptor-related protein., J. of Cell Science, 2000, 114 (Pt 5), 899-908.		
		OKUN V. et al., VLDL receptor fragments of different lengths bind to human rhinovirus HRV2 with different stoichiometry. An analysis of virus-receptor complexes by capillary electrophoresis., J. of Biological Chem., 2001, 276 (2), 1057-1062.		
		ORLANDO R. et al., Identification of the second cluster of ligand-binding repeats in megalin as a site for receptor-ligand interactions., PNAS(USA), 1997, 94 (6), 2368-2373.		
		PEACOCK S. et al., Human low density lipoprotein receptor expressed in Xenopus oocytes. Conserved signals for O-linked glycosylation and receptor-mediated endocytosis., J. of Biological Chem., 1988, 263 (16), 7838-7845.		
		PEARL F. et al., Assigning genomic sequences to CATH., Nucleic Acids Research, 2000, 28 (1), 277-282.		
		RETTENBERGER P. et al., Ligand binding properties of the very low density lipoprotein receptor. Absence of the third complement-type repeat encoded by exon 4 is associated with reduced binding of Mr 40,000 receptor-associated protein, J. of Biological Chem., 1999, 274 (13), 8973-8980.		
		RIECHMANN L. et al., Novel folded protein domains generated by combinatorial shuffling of polypeptide segments., PNAS, 2000, 97 (18), 10068-10073.		
		RONG L. et al., Conversion of a human low-density lipoprotein receptor ligandbinding repeat to a virus receptor: identification of residues important for ligand specificity, PNAS(USA), 1998, 95 (15), 8467-8472.		
		ROODVELDT et al. Directed evolution of proteins for heterologous expression and stability., Current Opinion in Structural Biology., 2005, Vol. 15, 50-56.		
		RUSSELL D. et al., Different combinations of cysteine-rich repeats mediate binding of low density lipoprotein receptor to two different proteins., J. of Biological Chem., 1989, 264 (36), 21682-21688.		
		SATO A. et al., 39-kDa receptor-associated protein (RAP) facilitates secretion and ligand binding of extracellular region of very-low-density-lipoprotein receptor: implications for a distinct pathway from low-density-lipoprotein receptor, Biochem., 1999, 341 (Pt 2), 377-383.		
		SAVONEN R. et al., The carboxyl-terminal domain of receptor-associated protein facilitates proper folding and trafficking of the very low density lipoprotein receptor by interaction with the three amino-terminal ligand-binding repeats of the receptor., J. of Biological Chem., 1999, 274 (36), 25877-25882.		
		SCHLEHUBER S. et al., A novel type of receptor protein, based on the lipocalin scaffold, with specificity for digoxigenin, J. Mol Biol., 2000, 297 (5), 1105-1120.		
		SCHLEHUBER S. et al., Duocalins: engineered ligand-binding proteins with dual specificity derived from the lipocalin fold., Biol. Chem., 2001, 382 (9), 1335-1342.		
		SCHLEHUBER S. et al., Tuning ligand affinity, specificity, and folding stability of an engineered lipocalin variant -- a so-called 'anticalin' -- using a molecular random approach., Biophysical Chem., 2002, 96 (2-3), 213-228.		

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		LI Y. et al., Differential functions of members of the low density lipoprotein receptor family suggested by their distinct endocytosis rates., J. of Biological Chem., 2001, 276 (21), 18000-18006.		
		LIU C. et al., Genomic organization of a new candidate tumor suppressor gene, LRP1B., Genomics, 2000, 69 (2), 271-274.		
		LIU C. et al., The putative tumor suppressor LRP1B, a novel member of the low density lipoprotein (LDL) receptor family, exhibits both overlapping and distinct properties with the LDL receptor-related protein., J. of Biological Chem., 2001, 276 (31), 28889-28896.		
		LIU Y. et al., Uptake of HIV-1 tat protein mediated by low-density lipoprotein receptor-related protein disrupts the neuronal metabolic balance of the receptor ligands., Nature Medicine, 2000, 6 (12), 1380-1387.		
		MAMMEN M. et al., Polyvalent Interactions in Biological Systems: Implications for Design and Use of Multivalent Ligands and Inhibitors, Angew. Chem., 1998, 37, 2754-2794.		
		MARTIN F. et al., A loop-mimetic inhibitor of the HCV-NS3 protease derived from a minibody.. Protein Engineering, 1999, 12 (11), 1005-1011.		
		MIKHAILENKO I. et al., Functional domains of the very low density lipoprotein receptor: molecular analysis of ligand binding and acid-dependent ligand dissociation mechanisms., J. of Cell Science, 1999, 112 (Pt 19), 3269-3281.		
		MOESTRUP S. et al., Megalin- and cubilin-mediated endocytosis of protein-bound vitamins, lipids, and hormones in polarized epithelia., Annu. Rev. Nutr., 2001, 21, 407-428.		
		NAKAYAMA M. et al., Identification of high-molecular-weight proteins with multiple EGF-like motifs by motif-trap screening., Genomics, 1998, 51 (1), 27-34.		
		NEELS J. et al., The second and fourth cluster of class A cysteine-rich repeats of the low density lipoprotein receptor-related protein share ligand-binding properties., J. of Biological Chem., 1999, 274 (44), 31305-31311.		
		NORD K. et al., Recombinant human factor VIII-specific affinity ligands selected from phage-displayed combinatorial libraries of protein A., Eur. J. Biochem., 2001, 268 (15), 4269-4277.		
		NORTH C. et al., Evidence that familial hypercholesterolemia mutations of the LDL receptor cause limited local misfolding in an LDL-A module pair., Biochemistry, 2000, 39 (43), 13127-13135.		
		NORTH C. et al., Solution structure of the sixth LDL-A module of the LDL receptor., Biochemistry, 2000, 39 (10), 2564-2571.		
		NORTH C. et al., Structural independence of ligand-binding modules five and six of the LDL receptor., Biochemistry, 1999, 38 (13), 3926-3935.		
		OBERMOELLER L. et al., Ca <sup>2+</sup> and receptor-associated protein are independently required for proper folding and disulfide bond formation of the low density lipoprotein receptor-related protein., J. of Biological Chem, 1998, 273 (35), 22374-22381.		
		OBERMOELLER L. et al., Differential functions of triplicated repeats suggest two independent roles for the receptor-associated protein as a molecular chaperone., J. of Biological Chem, 1997, 272 (16), 10761-10768.		

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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)		<b>Complete if Known</b>			
		<b>Application Number</b>	10/693,056		
		<b>Filing Date</b>	October 24, 2003		
		<b>First Named Inventor</b>	Kolkman, et al.		
		<b>Art Unit</b>	1639		
		<b>Examiner Name</b>	LIU, Sue Xu		
<b>Sheet</b>	<b>5</b>	<b>of</b>	<b>8</b>	<b>Attorney Docket No:</b> 022013-000160US	

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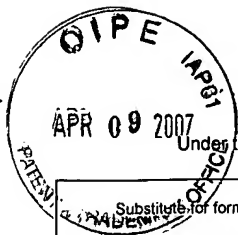
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		HOPFNER K. et al., New enzyme lineages by subdomain shuffling., PNAS(USA), 1998, 95, 9813-9818.	
		HORN I. et al., Molecular analysis of ligand binding to the second cluster of complement-type repeats of the low density lipoprotein receptor-related protein. Evidence for an allosteric component in receptor-associated protein-mediated inhibition of ligand binding., J. of Biology Chem., 1997, 272 (21), 13608-13613.	
		HOWELL BW. et al., The LDL receptor gene family: signaling functions during development., Current Opinion in Neuro., 2001, 11, 74-81.	
		HUANG W. et al., NMR solution structure of complement-like repeat CR8 from the low density lipoprotein receptor-related protein., J. of Biological Chem., 1999, 274 (20), 14130-14136.	
		HUDSON P. et al., High avidity scFv multimers; diabodies and triabodies., J. of Immunol. Methods, 1999, 231, 177-189.	
		HUSSAIN M. et al., The mammalian low-density lipoprotein receptor family., Annu. Rev. Nutr., 1999, 9, 141-172.	
		ISHII H. et al., cDNA cloning of a new low-density lipoprotein receptor-related protein and mapping of its gene (LRP3) to chromosome bands 19q12-q13. 2., Genomics, 1998, 51, 132-135.	
		JEON H. et al., Implications for familial hypercholesterolemia from the structure of the LDL receptor YWTD-EGF domain pair., Nature Struct Biology, 2001, 8 (6), 499-504.	
		JEON H. et al., Vesicle-reconstituted low density lipoprotein receptor. Visualization by cryoelectron microscopy., J. of Biological Chem., 2000, 275 (39), 30458-30464.	
		JERMUTUS L. et al., Tailoring in vitro evolution for protein affinity or stability., PNAS, 2001, 98 (1), 75-80.	
		KIM D. et al., Exon/intron organization, chromosome localization, alternative splicing, and transcription units of the human apolipoprotein E receptor 2 gene., J. of Biological Chem., 1997, 272 (13), 8498-8504.	
		KINGSLEY D. et al., Receptor-mediated endocytosis of low density lipoprotein: somatic cell mutants define multiple genes required for expression of surface-receptor activity., PNAS(USA), 1984, 81 (17), 5454-5458.	
		KOIDE A. et al., Probing protein conformational changes in living cells by using designer binding proteins: application to the estrogen receptor., PNAS, 2002, 99 (3), 1253-1258.	
		KOIDE A. et al., The fibronectin type III domain as a scaffold for novel binding proteins., J. Mol Biol., 1998, 284 (4), 1141-1151.	
		KOLKMAN J. et al., Directed evolution of proteins by exon shuffling., Nature Biotech., 2001, 19 (5), 423-428.	
		KRIEGER M. et al., The "best" of cholesterol, the "worst" of cholesterol: a tale of two receptors., PNAS(USA), 1998, 95 (8), 4077-4080.	
		KU J. et al., Alternate protein frameworks for molecular recognition., PNAS(USA), 1995, 92 (14), 6552-6556.	
		KURNIAWAN N. et al., NMR structure of a concatemer of the first and second ligand-binding modules of the human low-density lipoprotein receptor., Protein Science, 2000, 9 (7), 1282-1293.	

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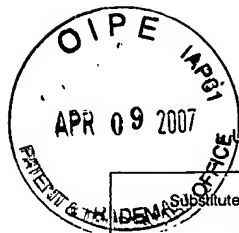
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		DOLEZAL O. et al., ScFv multimers of the anti-neuraminidase antibody NC10: shortening of the linker in single-chain Fv fragment assembled in V(L) to V(H) orientation drives the formation of dimers, trimers, tetramers and higher molecular mass multimers, Protein Engineering, 2000, 13 (8), 565-574.		
		DOLMER K. et al., NMR solution structure of complement-like repeat CR3 from the low density lipoprotein receptor-related protein. Evidence for specific binding to the receptor binding domain of human alpha(2)-macroglobulin, J. of Biological Chem, 2000, 275 (5), 3264-3269.		
		DUMOULIN M. et al., Single-domain antibody fragments with high conformational stability, Protein Science, 2002, 11 (3), 500-515.		
		ESSER V. et al., Mutational analysis of the ligand binding domain of the low density lipoprotein receptor, J. of Biological Chem., 1988, 263 (26), 13282-13290.		
		ESSER V. et al., Transport-deficient mutations in the low density lipoprotein receptor. Alterations in the cysteine-rich and cysteine-poor regions of the protein block intracellular transport, J. of Biological Chem., 1988, 263 (26), 13276-13281.		
		FASS D. et al., Molecular basis of familial hypercholesterolaemia from structure of LDL receptor module, Nature, 1997, 388 (6643), 691-693.		
		FITZGERALD D. et al., Pseudomonas exotoxin-mediated selection yields cells with altered expression of low-density lipoprotein receptor-related protein, J. of Cell Biology, 1995, 129 (6), 1533-141.		
		GOLDSTEIN J. et al., The cholesterol quartet, Science, 2001, 292 (5520), 1310-1312.		
		GOTZ M. et al., Ultrafast electron transfer in the complex between fluorescein and a cognate engineered lipocalin protein, a so-called anticalin, Biochemistry, 2002, 41 (12), 4156-4164.		
		GREENE, Host cell compatibility in protein expression, Methods in Molecular Biology., 2004, Vol. 267, 3-14.		
		GUNNERIUSSON E. et al., Affinity maturation of a Taq DNA polymerase specific affibody by helix shuffling, Protein Engineering, 1999, 12 (10), 873-878.		
		GUNNERIUSSON E. et al., Staphylococcal surface display of immunoglobulin A (IgA)- and IgE-specific in vitro-selected binding proteins (affibodies) based on Staphylococcus aureus protein A, App. Environ. Microbiol., 1999, 65 (9), 4134-4140.		
		HANES J. et al., Picomolar affinity antibodies from a fully synthetic naive library selected and evolved by ribosome display, Nature Biotech., 2000, 18 (12), 1287-1292.		
		HERZ J. et al., Lipoprotein receptors: beacons to neurons?, Trends in Neurosciences, 2001, 24 (4), 193-195.		
		HEWAT E. et al., The cellular receptor to human rhinovirus 2 binds around the 5-fold axis and not in the canyon: a structural view., EMBO Journal, 2000, 19 (23), 6317-6325.		
		HOILIGER P. et al., "Diabodies": small bivalent and bispecific antibody fragments., PNAS(USA). 1993, 90, 6444-6448.		

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		ADAMS G. et al., Generating improved single-chain Fv molecules for tumor targeting, J. of Immunol Methods, 1999, 231 (1-2), 249-260.	
		AGNELLO V. et al., Hepatitis C virus and other flaviviridae viruses enter cells via low density lipoprotein receptor, PNAS(USA), 1999, 96 (22), 12766-12771.	
		ANDERSEN A OM. et al., Identification of the minimal functional unit in the low density lipoprotein receptor-related protein for binding the receptor-associated protein (RAP). A conserved acidic residue in the complement-type repeats is important for recognition of RAP, J. of Biological Chem., 2000, 275 (28), 21017-21024.	
		ARNDT K. et al., A heterodimeric coiled-coil peptide pair selected in vivo from a designed library-versus-library ensemble, J. Mol Biol., 2000, 295 (3), 627-639.	
		AVRAMOGLU R. et al., Functional expression of the chicken low density lipoprotein receptor-related protein in a mutant chinese hamster ovary cell line restores toxicity of Pseudomonas exotoxin A and degradation of alpha2-macroglobulin, J. of Biological Chem., 1998, 273 (11), 6057-6065.	
		BEGLOVA N. et al., Backbone dynamics of a module pair from the ligand-binding domain of the LDL receptor, Biochemistry, 2001, 40 (9), 2808-2815.	
		BESTE G. et al., Small antibody-like proteins with prescribed ligand specificities derived from the lipocalin fold, PNAS(USA), 1999, 96 (5), 1898-1903.	
		BIERI S. et al., Folding, calcium binding, and structural characterization of a concatemer of the first and second ligand-binding modules of the low-density lipoprotein receptor, Biochemistry, 1998, 37 (31), 10994-11002.	
		BRANDES C. et al., Alternative splicing in the ligand binding domain of mouse ApoE receptor-2 produces receptor variants binding reelin but not alpha 2-macroglobulin, J. of Biological Chem., 2001, 276 (25), 22160-22169.	
		CONRATH K. et al., Camel single-domain antibodies as modular building units in bispecific and bivalent antibody constructs, J. of Biological Chem, 2001, 276 (10), 7346-7350.	
		DALY N. et al., Three-dimensional structure of a cysteine-rich repeat from the low-density lipoprotein receptor, PNAS(USA), 1995, 92 (14), 6334-6338.	
		DAVIS C. et al., Acid-dependent ligand dissociation and recycling of LDL receptor mediated by growth factor homology region, Nature, 1987, 326 (6115), 760-765.	
		DAVIS C. et al., The low density lipoprotein receptor. Identification of amino acids in cytoplasmic domain required for rapid endocytosis, J. of Biological Chem, 1987, 262 (9), 4075-4082.	
		DESMYTER A. et al., Antigen specificity and high affinity binding provided by one single loop of a camel single-domain antibody, J. of Biological Chem., 2001, 276 (28), 26285-26290.	
		DESMYTER A. et al., Three camelid VHH domains in complex with porcine pancreatic alpha-amylase. Inhibition and versatility of binding topology, J. of Biological Chem., 2002, 277 (26), 23645-23650.	
		DIMASI N. et al., Characterization of engineered hepatitis C virus NS3 protease inhibitors affinity selected from human pancreatic secretory trypsin inhibitor and minibody repertoires, J. of Virology, 1997, 71 (10), 7461-7469.	

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